

REMARKS

In the Office Action, claims 1-5 and 21-22 are rejected under 35 U.S.C. § 102; and claim 6 is rejected under 35 U.S.C. § 102 or, in the alternative, under 35 U.S.C. § 103. Claims 1 and 22 have been amended; claims 4-6 and 21 have been canceled without prejudice or disclaimer; and claim 23 has been newly added. Applicants respectfully submit that the rejections have been overcome or are improper in view of the amendments and for the reasons set forth below.

In the Office Action, claims 1-5 and 21-22 are rejected under 35 U.S.C. § 102. More specifically, claims 1-5 and 21-22 are rejected in view of International Patent Publication No. WO 98/06411 ("Guandalini"); claims 1-5 are rejected in view of International Patent Publication No. WO 95/33046 ("Morelli") in light of ATCC Catalogue; claims 1-5 are rejected in view of European Patent Document No. 861905 ("Pedraglio"); claims 1-5 are rejected in view of Tuomola et al.; claims 1-3 and 21-22 are rejected in view of U.S. Patent No. 5,603,930 ("Brassart"); and claims 1-3 and 21-22 are rejected in view of U.S. Patent No. 5,837,238 ("Casas").

As previously discussed, claim 1 has been amended and claim 23 has been newly added. In part, claims 1 and 23 essentially include the limitations of claim 6. Claims 2 and 22 depend from claims 1 and 23, respectively, where claims 4-6 and claim 21 have been cancelled without prejudice or disclaimer. Thus, the anticipation rejections with respect to claims 1-5 and 21-22 have been overcome and further should not be applied to new claim 23.

Accordingly, Applicants respectfully request that the anticipation rejection with respect to claims 1-5, 21 and 22 be withdrawn.

In the Office Action, claim 6 is rejected under 35 U.S.C. § 102 or, in the alternative, under 35 U.S.C. § 103 in view of Guandalini or Pedraglio or Tuomola or Brassart. Applicants believe that the anticipation rejection and alternative obviousness rejection have been overcome.

At the outset, claim 6 has been cancelled without prejudice or disclaimer and thus this rejection should be withdrawn with respect to same. Of the remaining pending claims at issue, claims 1 and 23 are the sole independent claims. Claim 1 recites a biologically pure culture of a lactic acid bacterium strain belonging to the genus *Lactobacillus* having a protection property against adhesion of pathogenic bacteria causing diarrhoea to intestinal cells and/or having a protection property against invasion of pathogenic bacteria causing diarrhoea into intestinal cells,

which *Lactobacillus* strain is capable of adhering to the intestinal mucosa of a host organism. Claim 1 essentially includes the features of originally filed claim 1 in addition to claim 2 as originally filed and further as supported in the specification, for example, on page 7 at paragraph 5 and page 15 at paragraph 4. Claim 1 further recites that the *Lactobacillus* strain is *Lactobacillus paracasei* CNCM I-2116. Independent claim 23 recites a food containing a biologically pure culture of a lactic acid bacterium strain belonging to the genus *Lactobacillus* that has essentially the same features as defined in claim 1.

The present invention relates to the specific *Lactobacillus paracasei* strain CNCM I-2116 (referred to herein as ST11) having a protection property against adhesion of pathogenic bacteria causing diarrhoea to intestinal cells (see, specification, Example 4) and/or having an active protection property against invasion of pathogenic bacteria causing diarrhoea into intestinal cells (see, specification, Example 5). Further, the *Lactobacillus* strain of the present invention is capable of adhering to the intestinal mucosa of the host organism and once implanted in the mucosa (or even before) can exert its beneficial effects, presumably by secreting metabolic compounds. See, specification, p. 7, paragraph 5.

The claimed *Lactobacillus* also exhibits an anti-allergenic property in that the strain has an impact on the synthesis of different immuno-modulating mediators. On one hand, ST11 strongly reduces IL-4 production in Th-2 type cells. This is a cytokine required for the secretion of IgE that is the major antibody class involved in allergic reactions. See, specification, p. 7, last paragraph to p. 8. At the same time on the other hand, the specific strain induces the Th-1 type that promotes cytokine IL-12 in antigen presenting cells (APCs) like macrophages and dendritic cells (see, specification, p. 8, paragraph 4) to further facilitate Th-1 type differentiation. Moreover, ST11 also promotes iNOS production that is a compound directed against intracellular pathogenic bacteria. See, specification, Example 10, Fig. 7.

In contrast, Applicants believe that the cited art is distinguishable from the claimed invention. With respect to Guandalini, this reference generally relates to a treatment of an acute infant's diarrhoea and to the prevention of allergic reactions in a subsequent phase. In this regard, Guandalini proposes administration of a specific *Lactobacillus* strain "GG", which *Lactobacillus* strain purportedly assists in re-hydration and/or re-nourishing of the affected patient. See, Guandalini, p. 7, lines 1-9.

Yet, nowhere does Guandalini disclose or suggest the specific *Lactobacillus paracasei* strain CNCM I-2116 as claimed. Further, Guandalini fails to describe a protection property against adhesion to and/or against invasion into intestinal cells of pathogenic bacteria provided by metabolic compounds secreted by the specific *Lactobacillus* strain as required by the claimed invention. Moreover, Guandalini fails to disclose or suggest the impact of the specific *Lactobacillus* strain as claimed on the immune cells and, for example, induction of iNOS. Thus, Applicants believe that Guandalini is clearly distinguishable from the claimed invention for at least these reasons.

Like Guandalini, the remaining cited references are distinguishable from the claimed invention. For example, nowhere do the remaining cited references disclose or suggest the specific *Lactobacillus paracasei* strain CNCM I-2116 as claimed. Further, the cited references fail to recognize a protection property against invasion into an intestinal cell of pathogenic bacteria and further fail to recognize the anti-allergenic property or induction of iNOS, let alone the properties of the specific *Lactobacillus* strain as claimed.

For example, Morelli generally relates to *Lactobacilli* strains and their use for treating a variety of gastrointestinal disorders, such as intestinal dismicrobism, ulcerative colitis, and diarrhoea of various origins. See, Morelli, p. 5, 1.12-17. Indeed, the activity of the strains against harmful bacteria is demonstrated in “co-culture experiments”, where a single strain and/or a mixture of the specific strains are exposed to the pathogen to inhibit its growth as further disclosed in Morelli.

Pedraglio relates to *Lactobacilli* strains useful in the treatment of various disorders of the gastrointestinal tract, such as peristaltic disorders, gastroenteritis, heartburn, flatulence and diarrhoea. In particular, these strains are used to reconstitute the intestine following administration of antibiotics (Pedraglio, p. 6, 1. 7-8) or after anti-tumour radiotherapy (Pedraglio, p. 5, 1.10). Additionally, activity opposing “pathogens” described as lowering the pH of the intestinal environment (Pedraglio, p. 4, 1. 33-35).

Tuomola describes in vitro experiments related to the adhesion of *Lactobacilli* strains to CaCo-2 cells compared to Na-azide killed E. coli. See, Tuomola, p. 46, col. 2, 24-30. As a result, none of the tested strains adhered more effectively to CaCo-2 cells than control strains. See, Tuomola, p. 50, 1. 29-32.

Brassant relates to *Lactobacilli* and in particular to the *Lactobacillus johnsonii* strain CNCM I-1225 which adheres to CaCo-2 cells and apparently inhibits adhesion of pathogenic bacteria by competitive exclusion. See, Brassant, col. 2, 1. 3-4. Casas discloses a method for treating acute diarrhoea (Casas, col. 2, 1. 1-3) largely caused by rotaviruses (see, Casas, abstract), by administering *Lactobacillus reuteri*. Casas demonstrates that *L. reuteri* colonizes the gastrointestinal tract of patients.

Even if combinable, the cited art is deficient with respect to the specific *Lactobacillus* strain and properties thereof as claimed. Nowhere does the cited art disclose or suggest the specific *Lactobacillus paracasei* strain CNCM I-2116 as claimed, let alone a protection property against adhesion to and/or against invasion into intestinal cells of pathogenic bacteria provided by metabolic compounds secreted by the specific *Lactobacillus* strain as further required by the claimed invention. Moreover, nowhere does the cited art disclose or suggest the impact of the specific *Lactobacillus* strain as claimed on the immune cells and, for example, induction of iNOS.

Based on at least these differences between the cited art and the claimed invention as discussed above, Applicants believe that the cited art is distinguishable from the claimed invention. Therefore, Applicants respectfully submit that the cited art, even if combinable, fails to anticipate and render obvious the claimed invention.

Accordingly, Applicants respectfully request that the anticipation and obviousness rejections be withdrawn.

For the foregoing reasons, Applicants respectfully submit that the present application is in condition for allowance and earnestly solicit reconsideration of same.

Respectfully submitted,

BELL, BOYD & LLOYD LLC

BY 

Robert M. Barrett
Reg. No. 30,142
P.O. Box 1135
Chicago, Illinois 60690-1135
Phone: (312) 807-4204

Dated: July 8, 2004